REMARKS

Claims 1-11, 14-25, 28-35, 44, 45, and 69-74 are pending in the application. Claims 1 and 70 are currently amended. Claims 75-78 are new claims.

Claim 70 has been amended to delete the word "substantially," as suggested by the Office to overcome the 35 U.S.C. §112 second paragraph rejection of claims 70-74. Claims 1 and 70 have also been amended to delete the word "thermostable."

The Conclusion on page 11 of the current Office Action states that none of the claims are presently allowable; however, neither does the Office present a formal rejection of claims 6-11. New claims 75-78 have been added to restate the subject matter of claims 6-9 with slight differences in scope. We respectfully observe that these claims 6-11 and 75-78 identify with specificity particular sequences including SEQ ID NOS. 4, 5 and 7. Claim 10 is an independent claim that has not been formally rejected, but is also not found to be allowable. Applicant's attorney respectfully solicits an indication that these claims are allowable.

Claims 1-5, 14-25, 28-35, 44, 45, and 69-74 stand rejected under 35 U.S.C. §112, first paragraph for nonenablement. The Office holds that the claims are enabling for the species including the sequences that are specifically disclosed, but not for a broader range of subject matter that is encompassed by the rejected claims, i.e., the scope of the claims is broader than the scope of enablement. The Office cites *In re Wands* for a list of factors that are relevant to the enablement issue.

At issue in *Wands* was whether a deposit of living cells was required to provide enablement for claims that addressed, broadly, a screening assay where IgM antibody had a binding affinity constant for HBsAg. The disclosure taught how to make and perform

this assay from starting materials using mice, HBsAg antigen, and myeloma cells, but not from a universe of other materials. The Federal Circuit ultimately determined that enablement did exist for the broad concept, even where there was no deposit and the disclosed method taught narrowly the use of mice and myeloma cells. Thus, the analogy to *Wands* fails to the extent that the Office concludes a wide-ranging disclosure of multiple embodiments and multiple means is always required to support broad claims, even genus claims, and that broad claims can never be supported by a single disclosed embodiment.

While the *Wands* factors are helpful, the factors merely guide one to a conclusion on the facts of each case. The ultimate issue is one of assessing reasonableness whether experimentation is undue in light of the state of the art and the level of ordinary skill. The factors are merely a guide towards this end:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. [19] However, experimentation needed to practice the invention must not be undue experimentation. [20] "the key word is 'undue,' not 'experimentation.' " [21]
>
> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *Ansul Co. v. Uniroyal, Inc.* [448 F.2d 872, 878-79; 169 USPQ 759, 762-63 (2d Cir. 1971), cert. denied , 404 U.S. 1018 [172 USPQ 257] (1972)]. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed * * * . [22]
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> The term "undue experimentation" does not appear in the statute, but it is well established that enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. [23] Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations. The board concluded that undue experimentation would be needed to practice the invention on the basis of experimental data presented by Wands. These data are not in dispute. However, Wands and the board disagree strongly on the conclusion that should be drawn from that data.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman . [24] They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Presently, the Office takes a position that only SEQ ID NOS. 1, 2, 4, 5, and 7 are disclosed, but Applicant has not provided guidance, knowledge or rationale, as to which amino acids are tolerant of modification. The Office identifies several areas of specific concern, such as protein folding, percent homologies, excessive screening required to prove successful modifications, and retention of functionality in the modified proteins.

It is error for the Office to assert that the disclosure teaches nothing germane to the scope of the claims other than, specifically, SEQ ID NOS. 1. 2, 4, 5, and 7. This is because the disclosure also teaches the use of family GH48, CBDII and CBDIII domains in combination. We refer to the attached declaration of Dr. Himmel, which shows that a working knowledge of domain families is an essential tool for practitioners in this art. The Declaration provides evidence of 16 GH48 family enzymes, 125 instances of CBDII domains, and 66 instances of CDBIII domains listed in the CAZy site index, with cross-reference to other databases including GenBank and SwisProt from which similar search results may be obtained. These elements identified in CAZy can be combined in approximately 132,000 different combinations of three elements (16 X 125 X 66). The number is approximate because some of the sequences are not fully disclosed but could be fully characterized with routine effort. The guidance provided by the specification is to combine these families as recited in the broader claims. Although the exact sequences are not specifically disclosed in the present specification except by reference to family

names, it is sufficient in this art to provide guidance directing practitioners to the combination of well known domain families. "A patent need not teach, and preferably omits, what is well known in the art." *In re Buchern*, 929 F.2d 660, 661 (Fed. Cir. 1991).

By analogy to *Wands*, the present Specification provides guidance to approximately 132,000 combinations of reported domains. It is within the level of ordinary skill to make these combinations as directed and claimed, just as it was within the level of ordinary skill in *Wands* to practice a broadly claimed invention but on the basis of fewer known combinations. Contrary to the Office assertion that screening would be required to confirm functionality in the recombinant peptides, publications like Ngo et al. and Birkhauser merely indicate that there is some uncertainty with functional success so that it is routine to screen recombinant peptides for functionality. According to *Wands*, screening is permissible and does not preclude enablement if it is routine in the art, as is the present case.

In light of the foregoing arguments, we respectfully request withdrawal of the §112 first paragraph rejection affecting claims 1-5, 14-25, 28-35, 44, 45, and 69-74.

Claims 1-5, 14-25, 28-35, 44, 45, and 69-74 stand rejected under 35 U.S.C. §112 first paragraph because Applicant has not shown possession of the claimed invention. This type of rejection is sometimes alternatively referred to as that of 'written description.' The Federal Circuit acknowledges confusion between the respective enablement and written description requirements, but also that the standards are related and intertwined:

> There appears to be some confusion in our decisions concerning the extent to which the "written description" requirement is separate and distinct from the enablement requirement. . . .

> . . .This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116-1117 (Fed. Cir 1991).

As to written description, the Office observes Applicant's citation of *Enzio Biochem*, but chooses to distinguish the application of *Enzio* on the specific facts of this case. The case actually cited in the prior response cited was *Amgen*, but the quoted passage did rely upon *Enzio*. *Amgen* was cited for the principle that it is not necessary to enunciate each and every species encompassed by a genus claim. The issue of written description devolves to Office allegations that the application discloses a species but claims a genus. The Office now agrees that a genus claim may be supported by a representative number of disclosed species--not all species within a genus need be specifically disclosed. Thus, Applicant is satisfied that there is agreement as to the law.

We fail to understand how the Office distinguishes the Enzio/Amgen premise of law on the facts of this case. The guidance to use combinations of domain families leads inevitably to a huge number of combinations. Dr. Himmel's declaration provides evidence that something like 132,000 combinations of structure are obtainable within the level of ordinary skill from the broad guidance and knowledge imparted by the present Specification. Surely this is a representative number of species to support a genus claim.

Therefore, we respectfully traverse the 'possession of the invention' rejection and request it to be withdrawn.

Again, the Office refers to written description guidelines located generally at www.uspto.gov. We are unable to find the specific guidelines and again request the Office to particularly identify a citation if they are relevant to this prosecution. Availing the Internet to arrive at USPTO.gov and entering "written description" in the search engine there located, produces an error message stating the search request has identified more than 1000 documents so it will be necessary to narrow the search.

Claims 28-35, 44, and 45 stand rejected under 35 U.S.C. §112 first paragraph. This rejection is stated because the claims recite identity with specifically disclosed sequences ranging from 70% to 90% identity. The Office asserts that there is substantial variation within the claimed genus, so one must describe a representative number of species in support of the genus. The representative number of species must relate functionality to relevant identifying characteristics, such as structural, physical, or chemical properties. This is precisely what Applicant has done, for example, beginning at line 12 on page 19 of the Specification where there is a suggestion to make conservative substitutions of like-functioning residues, and on page 20 where fusion proteins are discussed, so it cannot be said that such guidance is absent.

The Office further alleges that claims 8-35, 44, and 45 read upon a wide variety of functionally unrelated compositions and that the modified peptide sequences would have a diverse range of functionalities. We fail to understand the relevancy of the Office position, because a wide range of utilities are also disclosed and it is permissible for a species or genus of composition to have a wide range of functionality. A selection of useful modified peptides may be made based upon the claimed sequences, for example, as recited in the paragraph beginning at line 23 on page 20. Even if the modification of a

peptide sequence results in rendering the peptide nonfunctional for its natural purpose, such peptides also have utility, for example, in fully characterizing the domain or in selectively blocking activity of the peptide in a competitive assay, which may be performed according to the last paragraph on page 17 of the Specification.

For the reasons stated above, Applicant's attorney respectfully solicits allowance of all the claims.

Applicant's attorney respectfully solicits a Notice of Allowance in this application. The Commissioner is authorized to charge any additionally required fees to deposit account 14-0460. Should the Examiner have any questions, comments, or suggestions that would expedite the prosecution of the present case to allowance, Applicants' representative, Paul White, earnestly requests a telephone call at (303) 384-7575.

Respectfully submitted

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